

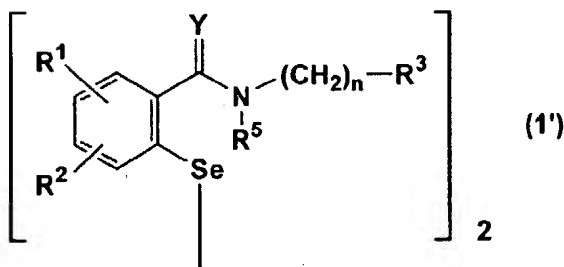
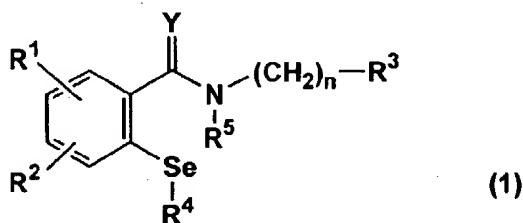
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-12 (Canceled)

Claim 13 (Previously Presented): A method for reduction of a substrate with thioredoxin reductase, comprising combining the thioredoxin reductase, the substrate and NADPH under conditions to reduce the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

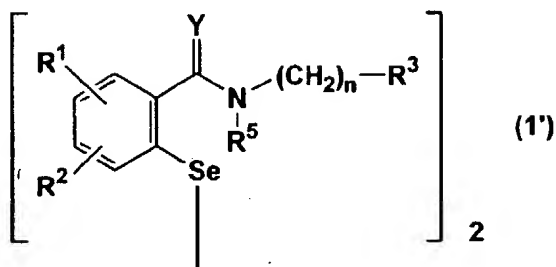
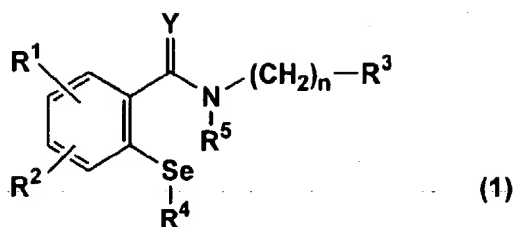


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wherein R¹ and R² independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C₁-C₆ alkyl group, or a C₁-C₆ alkoxy group, or R¹ and R² may combine together to represent methylenedioxy group; R³ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R⁴ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R⁵ represents a hydrogen atom or a C₁-C₆ alkyl group, or R⁴ and R⁵ may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 14 (Previously Presented): The method according to claim 13 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benziso-selenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

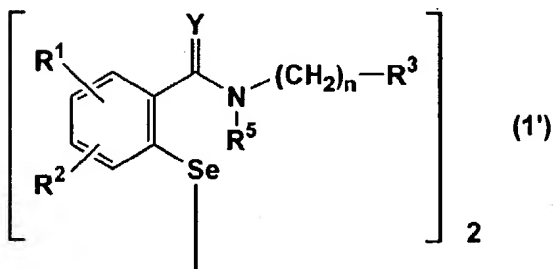
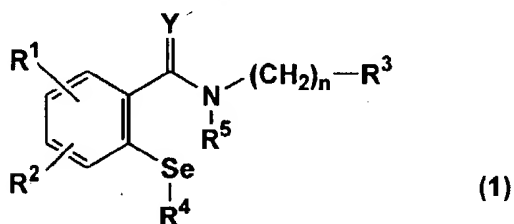
Claim 15 (Currently Amended): A method of enhancing peroxidase activity of thioredoxin reductase, comprising combining NADPH, thioredoxin reductase, thioredoxin and a substrate under conditions to enhance peroxidase activity of thioredoxin reductase, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxy group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S- glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 16 (Previously Presented): The method according to claim 17 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benzisoselenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

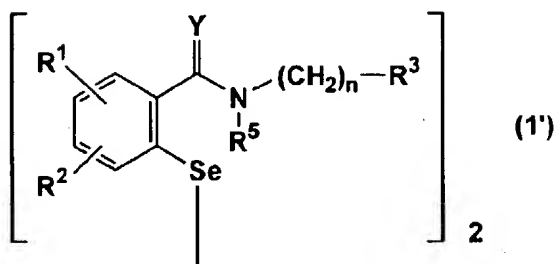
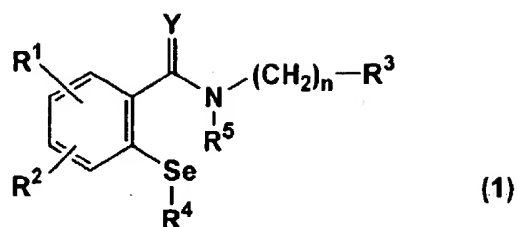
Claim 17 (Currently Amended): A method of oxidizing reduced thioredoxin by a substrate, the method comprising combining reduced thioredoxin and a substrate under conditions to oxidize the reduced thioredoxin with the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



wherein R¹ and R² independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C₁-C₆ alkyl group, or a C₁-C₆ alkoxy group, or R¹ and R² may combine together to represent methylenedioxy group; R³ represents an aryl group, an aromatic heterocyclic

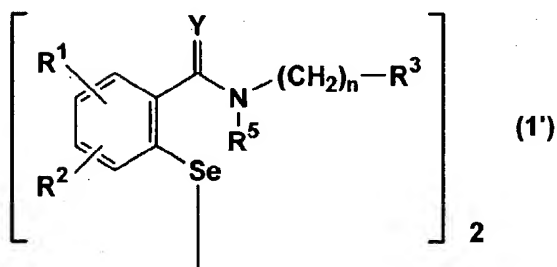
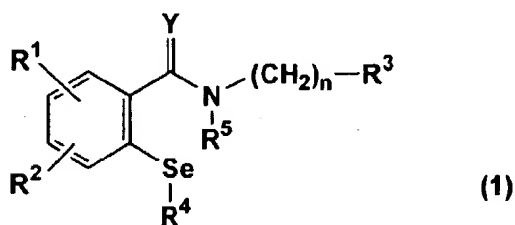
group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 18 (Currently Amended): A method for reducing a peroxide comprising ~~oxidizing reduced thioredoxin in a peroxidase reaction wherein the thioredoxin has been reduced by thioredoxin reductase and NADPH in the presence in a substrate~~ combining thioredoxin, thioredoxin reductase, NADPH and a substrate under conditions to reduce the peroxide, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxy group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

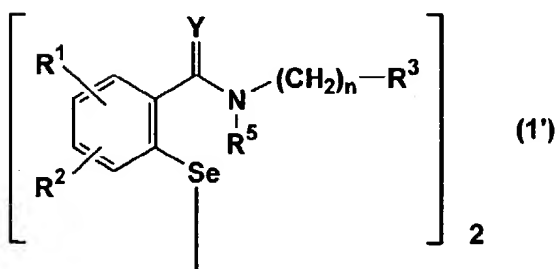
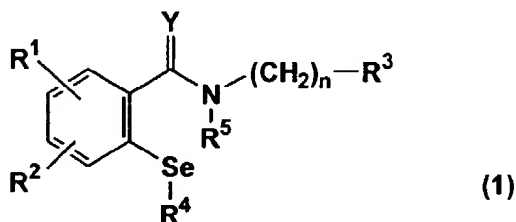
Claim 19 (Currently Amended): A method of preventing peroxidation of a substance comprising combining thioredoxin, thioredoxin reductase and NADPH with a substrate under conditions to prevent peroxidation of the substance, the substrate ~~comprising a substance~~ being selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxy group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be

substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 20 (Previously Presented): A method for enhancing peroxidase activity of thioredoxin reductase in vivo which comprises administering a peroxidase activity enhancing effective amount of a substrate to a mammal, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

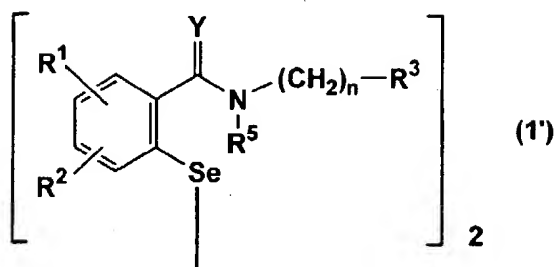
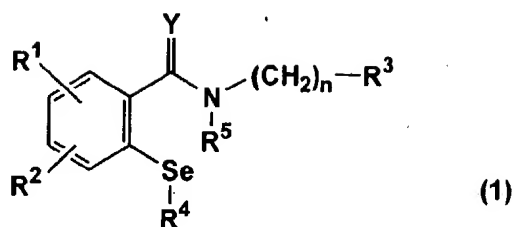


wherein R¹ and R² independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C₁-C₆ alkyl group, or a C₁-C₆ alkoxy group, or R¹ and R² may combine together to represent methylenedioxy group; R³ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R⁴ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R⁵ represents a hydrogen atom or a C₁-C₆ alkyl group, or R⁴ and R⁵ may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 21 (Previously Presented): The method according to claim 20 wherein the mammal is a human.

Claim 22 (Previously Presented): A method of reducing a peroxide in vivo which comprises administering an peroxide reducing effective amount of a substrate to a mammal, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula

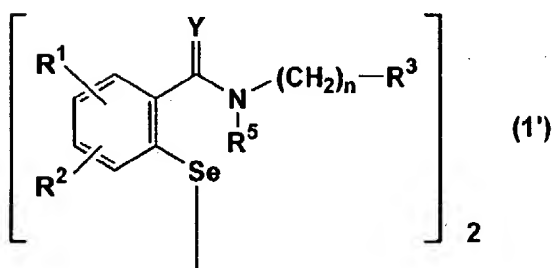
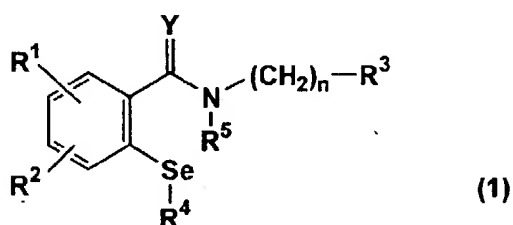
(1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxy group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 23 (Previously Presented): The method according to claim 22 wherein the mammal is a human.

Claim 24 (Currently Amended): A method of preventing peroxidation of a substance in vivo by oxidizing reduced thioredoxin in a peroxidase reaction proceeded by thioredoxin reductase comprising administering a peroxidation preventing effective amount of a substrate to a mammal, the substrate ~~comprising a substance~~ being selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



wherein R¹ and R² independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C₁-C₆ alkyl group, or a C₁-C₆ alkoxy group, or R¹ and R² may combine together to represent methylenedioxy group; R³ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R⁴ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α-amino acid group, or an aralkyl group whose aryl moiety may be

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substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1-C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 25 (Previously Presented): The method according to claim 24 wherein the mammal is a human.